A simple clinical tool for stratifying risk of clinically significant chronic kidney disease after nephrectomy: development and multinational validation

Supplementary Material

Supplementary Table 1 – Numbers of participants excluded according to prespecified criteria

Exclusion Criteria	Derivation Cohort	Validation Cohort 1	Validation Cohort 2	Validation Cohort 3	Validation Cohort 4	Exploratory Analysis
Missing preoperative eGFR	7 (2)	418 (46)	21 (15)	2 (3)	0 (0)	3 (<1)
Missing postoperative eGFR	39 (14)	127 (14)	24 (17)	0 (0)	0 (0)	2,765 (99)
Abnormal contralateral kidney	13 (5)	18 (2)	0 (0)	0 (0)	0 (0)	0 (0)
Non-surgical management	69 (24)	160 (18)	3 (2)	0 (0)	0 (0)	0 (0)
Preoperative eGFR <60	159 (55)	191 (21)	69 (49)	58 (97)	47 (100)	32 (<1)
Kidney replacement therapy	0 (0) [a]	0 (0) [a]	16 (11)	0 (0)	0 (0)	0 (0)
Previous nephrectomy	0 (0) [b]	0 (0) [b]	9 (6)	0 (0)	0 (0)	0 (0)
Total Excluded (% of total)	287 (29)	914 (68)	142 (44)	60 (23)	47 (18)	2,800 (60)
Total Included (% of total)	699 (71)	423 (32)	179 (56)	205 (77)	221 (82)	1,866 (40)
Total (included and excluded)	986	1,337	321	265	268	4,666

Data presented as count (% of all excluded patients within respective cohort), unless specified.

[a] Patients undergoing kidney replacement therapy were considered in the preoperative eGFR <60 mL/min per 1.73m^2 category.

[b] Patients who had previously been diagnosed/managed for kidney cancer were not included in these datasets. Patients who had undergone nephrectomy for an indication other than kidney cancer were excluded under the abnormal contralateral kidney criterion.

eGFR, estimated glomerular filtration rate (in mL/min per 1.73m^2).

Supplementary Table 2 – Patient and tumour characteristics

	Derivation Cohort [a] n (%) n = 699	Validation Cohort 1 [b] n (%) n = 423	Validation Cohort 2 [c] n (%) n = 179	Validation Cohort 3 [d] n (%) n = 205	Validation Cohort 4 [e] n (%) n = 221
Age					
Median [IQR]	60 [52-68]	61 [53-69]	57 [46-66]	59 [49-68]	62 [53-69]
<65yrs	467 (67)	261 (62)	131 (73)	129 (63)	128 (58)
≥65yrs	232 (33)	162 (38)	48 (27)	76 (37)	93 (42)
Sex					
Female	234 (33)	169 (40)	70 (39)	80 (39)	73 (33)
Male	465 (67)	254 (60)	109 (61)	125 (61)	148 (67)
Diabetes mellitus					
No	594 (85)	356 (84)	148 (83)	182 (89)	198 (88)
Yes	105 (15)	67 (16)	31 (17)	23 (11)	26 (12)
Preoperative eGFR					
Median [IQR]	87 [76-98]	86 [73-97]	87 [74-102]	85 [73-97]	88 [80-97]
60-69	92 (13)	78 (18)	30 (17)	42 (20)	21 (10)
70-79	157 (22)	89 (21)	32 (35)	41 (20)	36 (16)
80-89	141 (20)	95 (22)	38 (21)	43 (21)	61 (28)
≥90	309 (44)	161 (38)	79 (44)	79 (39)	103 (46)
Nephrectomy type					
Partial	187 (27)	136 (32)	65 (37)	76 (37)	109 (49)
Radical	512 (73)	287 (68)	113 (63)	129 (63)	112 (51)
T-Stage [f]					
Benign	-	-	10 (6)	-	17 (8)
T1	449 (64)	291 (69)	103 (58)	152 (74)	138 (62)
T2	49 (7)	32 (8)	19 (11)	37 (18)	13 (6)
T3/4	200 (29)	100 (24)	47 (26)	2 (1)	51 (23)
Missing	1 (<1)	-	-	14 (7)	2 (1)
Tumour size					
<40 mm	284 (41)	185 (44)	85 (47)	67 (33)	107 (48)
40-70 mm	246 (35)	146 (35)	50 (28)	89 (43)	67 (30)
>70 mm	112 (16)	58 (14)	44 (25)	35 (17)	44 (20)
Missing	57 (8)	34 (8)	-	14 (7)	3 (2)

[a] Patients with RCC from Queensland (Australia) managed surgically between Jan 2012 and Dec 2013 (n=699).

[b] Patients with RCC from Victoria (Australia) managed surgically between Jan 2012 and Dec 2013 (n=423).

[c] Patients with kidney tumours managed surgically at Princess Alexandra Hospital (Queensland, Australia) between June 2013 and Jan 2018 (n=179).

[d] Patients with kidney tumours managed at Western General Hospital (Edinburgh, Scotland) between January 2002 and December 2013 (n=205).

[e] Validation Cohort 4: Patients with kidney tumours managed surgically at Frimley Park Hospital (England) between January 2010 and December 2018 (n=221).

[f] Clinical T-stage was reported for the derivation cohort; pathological T-stage was reported for the remaining cohorts.

eGFR, estimated glomerular filtration rate (in mL/min per 1.73m^2); IQR, interquartile range; RCC, renal cell carcinoma.

Supplementary Table 3 – Logistic regression analysis considering risk strata as the independent variable

	Odds Ratio [a] (95% CI)	Number of Events (*n*, %)				
		Derivation Cohort [a]	Validation Cohort 1 [b]	Validation Cohort 2 [c]	Validation Cohort 3 [d]	Validation Cohort 4 [e]
Risk Stratum (Points)						
Negligible (0-3)	0.04 (0.00 to 0.33)	1 (<1)	4 (2)	1 (1)	0 (0)	2 (2)
Low (4-6)	1.00	13 (8)	10 (9)	5 (15)	7 (13)	2 (3)
Moderate (7-8)	3.18 (1.63 to 6.19)	40 (21)	27 (23)	10 (24)	14 (26)	9 (20)
High (9-10)	10.15 (4.81 to 21.44)	30 (46)	30 (61)	8 (47)	19 (68)	9 (69)
Intercept	0.08 (0.05 to 0.149)					
Per Point	1.89 (1.63 to 2.19)					

Percentages reflect number of events within each risk stratum.

[a] Derivation Cohort: Patients with RCC from Queensland (Australia) managed surgically between Jan 2012 and Dec 2013 (*n*=699).

[b] Validation Cohort 1: Patients with RCC from Victoria (Australia) managed surgically between Jan 2012 and Dec 2013 (*n*=423).

[c] Validation Cohort 2: Patients with kidney tumours managed surgically at the Princess Alexandra Hospital (Brisbane, Queensland, Australia) between June 2013 and Jan 2018 (*n*=179).

[d] Validation Cohort 3: Patients with kidney cancer managed surgically at the Western General Hospital (Edinburgh, Scotland) between January 2002 and December 2012 (*n*=205).

[e] Validation Cohort 4: Patients with kidney tumours managed surgically at the Frimley Park Hospital (England) between January 2010 and December 2018 (*n*=221).

CI, confidence interval.

Supplementary Table 4 – Characteristics of living kidney donors

	$n = 1,866$
Age—years	
Median [IQR]	51 [43-59]
<65	1,697 (91)
≥65	169 (9)
Sex	
Female	1,100 (59)
Male	766 (41)
Diabetes mellitus	
No	1,854 (99)
Yes	12 (<1)
Preoperative eGFR—mL/min per 1.73m^2	
Median [IQR]	92 [82-102]
60-69	107 (6)
70-79	300 (16)
80-89	411 (22)
≥90	1,048 (56)

eGFR, estimated glomerular filtration rate; IQR, interquartile range

Supplementary Table 5 – Risk prediction models in the derivation cohort with odds ratios reported

	Univariable OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age—years				
<65	1	1	1	1
≥65	4.43 (2.74-7.17)	1.93 (1.12-3.32)	1.95 (1.13-3.32)	1.93 (1.12-3.32)
Sex				
Female	1	1	1	
Male	1.30 (0.79-2.14)	1.09 (0.63-3.74)	1.08 (0.63-1.88)	—
Diabetes mellitus				
No	1	1	1	1
Yes	1.80 (1.02-3.16)	1.92 (0.96-3.74)	1.84 (0.92-3.71)	1.93 (0.96-3.86)
Preoperative eGFR—mL/min per 1.73m^2				
60-69	30.88 (14.88-64.07)	23.33 (8.41-64.07)		23.57 (8.58-64.72)
70-79	15.33 (7.46-31.82)	11.13 (4.17-29.96)	—	11.13 (4.17-29.96)
80-89	6.04 (2.77-13.20)	5.75 (2.01-16.44)		5.81 (2.05-16.28)
≥90	1	1		1
Preoperative eGFR—mL/min per 1.73m^2				
Per unit	0.91 (0.89-0.93)	—	0.92 (0.89-0.94)	—
Nephrectomy Type				
Partial	1	1	1	1
Radical	6.62 (1.07-16.61)	6.04 (2.22-16.44)	6.11 (2.27-16.44)	5.99 (2.22-16.11)
Intercept	—	0.00 (0.00-0.001)	16.78 (1.91-148.41)	0.00 (0.00-0.01)

Data presented as odds ratio (OR) and 95% confidence interval (CI). Estimates calculated using logistic regression models. All variables included in models presented above; (—) indicates a variable was excluded from the respective model. eGFR, estimated glomerular filtration rate.
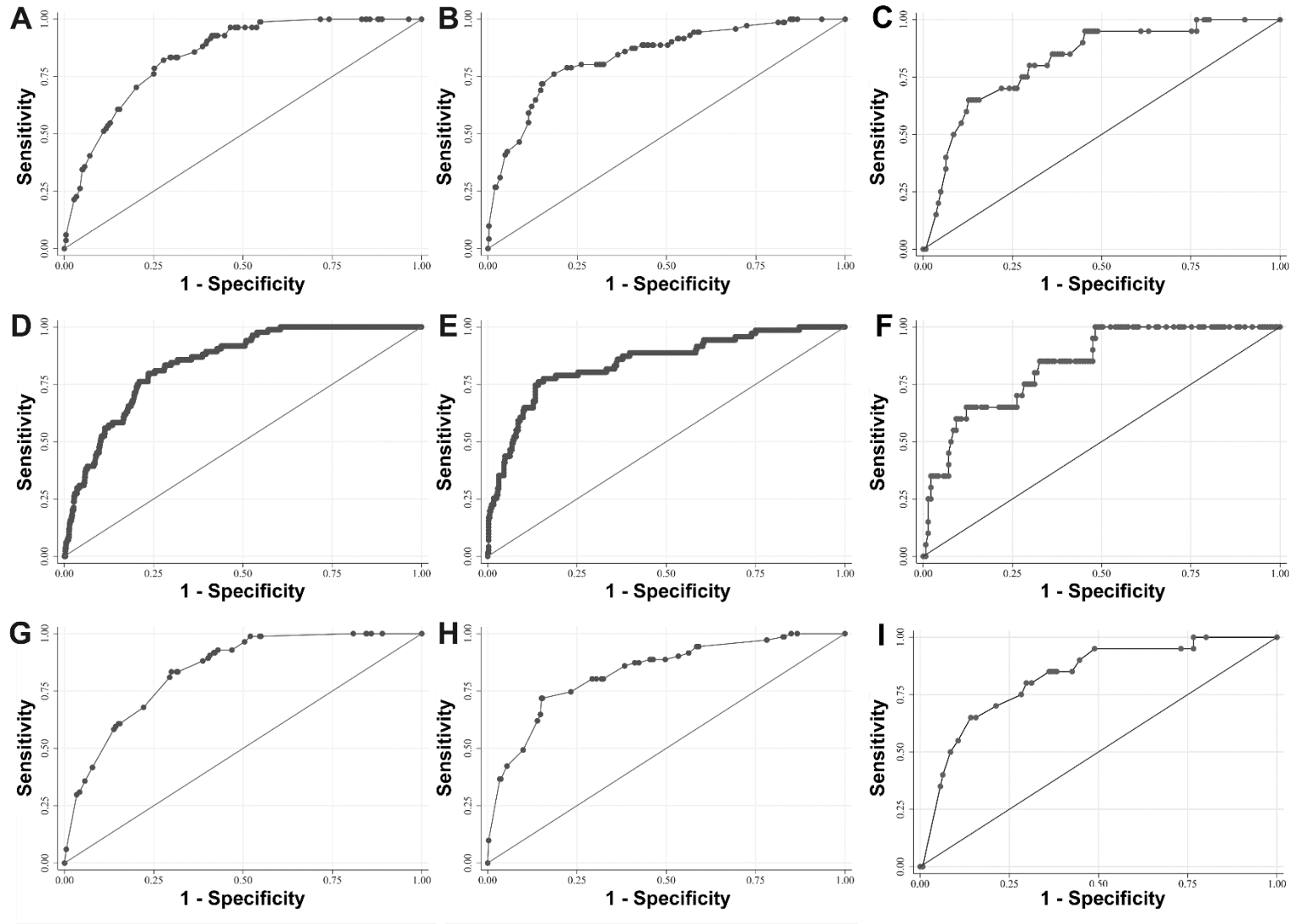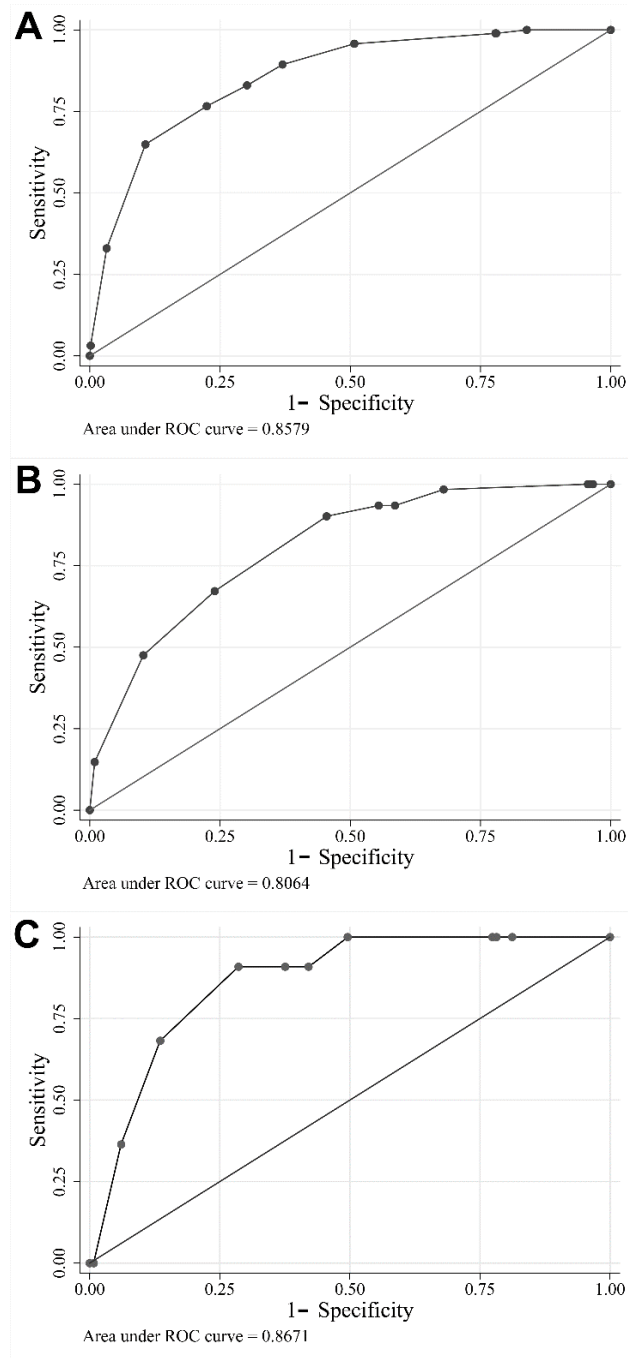
Supplementary Figure 1

Receiver operating characteristics curves for Models 1-3 (Table 1). **Model 1: A** derivation cohort (*C* = 0.84), **B** validation cohort 1 (*C* = 0.84), **C** validation cohort 2 (*C* = 0.82). **Model 2: D** derivation cohort (*C* = 0.84), **E** validation cohort 1 (*C* = 0.84), **F** validation cohort 2 (*C* = 0.84). **Model 3: G** derivation cohort (*C* = 0.84), **H** validation cohort 1 (*C* = 0.83), **I** validation cohort 2 (*C* = 0.82).
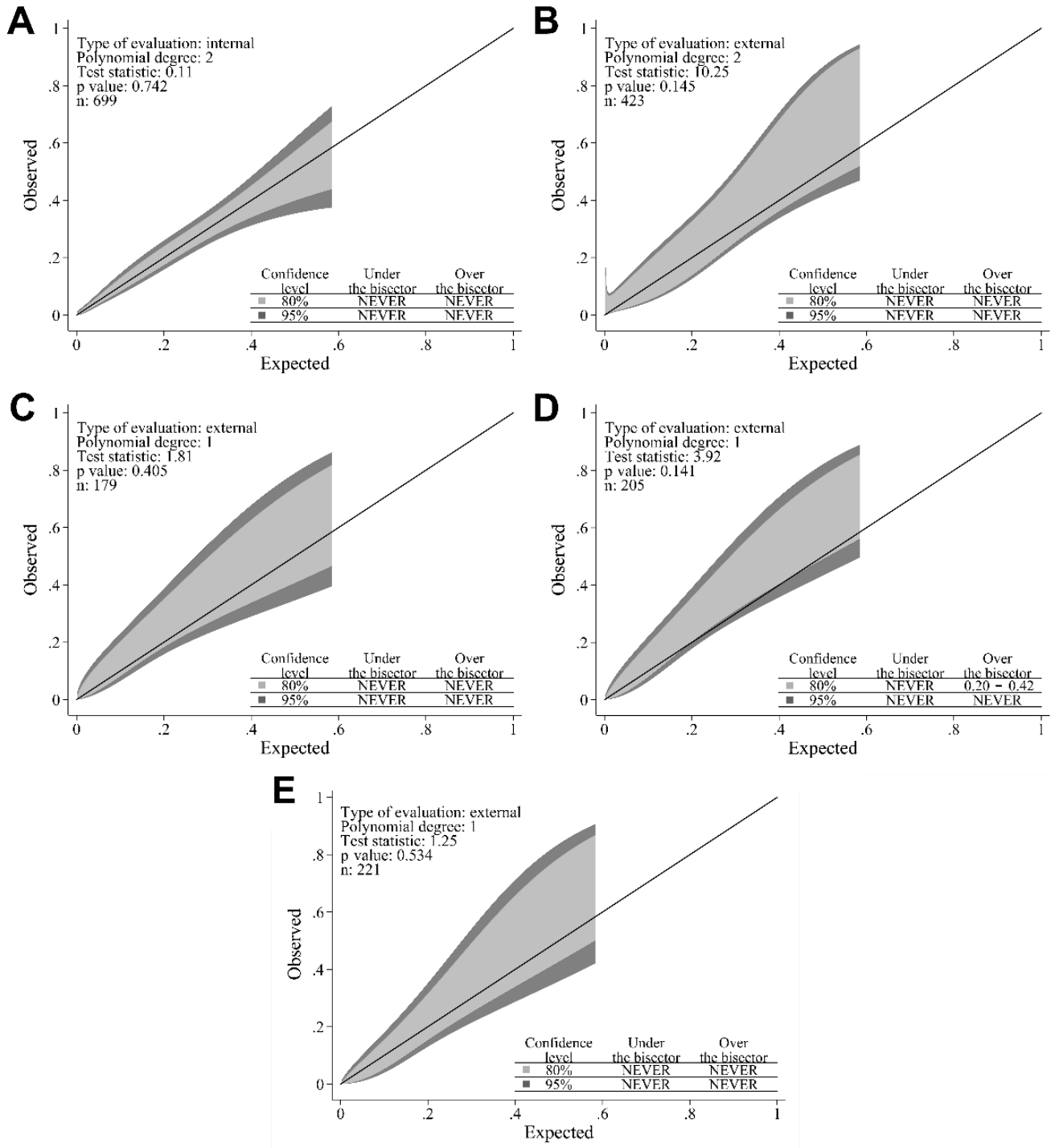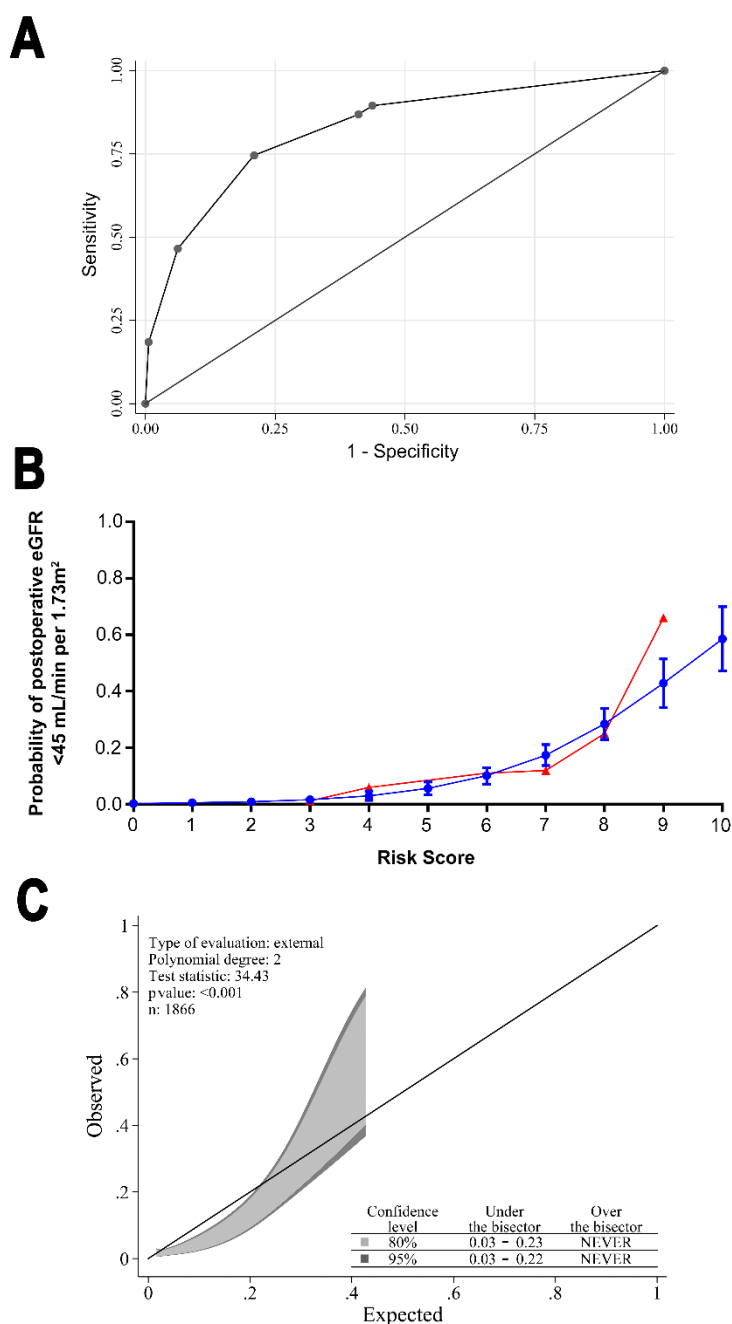
Supplementary Figure 2

Calibration belt plots for the clinical score model in the derivation and validation cohorts, showing calibration at various confidence levels. **A:** Derivation cohort; **B:** validation cohort 1; **C:** validation cohort 2; **D:** validation cohort 3; **E:** validation cohort 4.

Supplementary Figure 3

Receiver-operating characteristics curves for the clinical score model in sensitivity analyses. **A**: Patients with stage T1 tumours in derivation cohort and validation cohort 1 ($C = 0.86$); **B**: Patients with stage T2-4 tumours in derivation cohort and validation cohort 1 ($C = 0.81$); **C**: Patients from validation cohort 2, excluding 24 patients who presumably overlapped with the derivation cohort (data were deidentified so overlap was not able to be confirmed) ($C = 0.87$).

Supplementary Figure 4

Discrimination and calibration of the clinical score model in living kidney donors. **A**: Receiver-operating characteristics curve, $C = 0.83$. **B**: Observed absolute risk (red) and predicted probability (blue) of postoperative estimated glomerular filtration rate (eGFR) <45 mL/min per 1.73m^2 plotted against clinical score. **C**: Calibration belt (demonstrating overestimation of likelihood when predicted probability was less than 0.2).